



SIGNIFICANCE OF BETA-HCG EXPRESSION IN CYSTIC DISEASE OF BREAST

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ABSTRACT

Introduction- Gross breast cysts filled with serous fluid are almost always benign, yet the bearers of such cysts are at four times greater risk of developing a malignancy in the breast. Two forms of benign breast disease have the greatest clinical interest, either for their relationship to neoplasm or for their appearance during particular periods of a woman's maturity **Materials and Method-** This study was conducted in Dr. B.R.A.M. Hospital, Raipur in Department of General Surgery from February 2024 to February 2025. This is a prospective analytical study. Total sample size taken is 50. **Conclusion-** The finding indicated that the breast cyst of size 1-2cm are majorly having clear fluid, significantly less amount of beta hCG and benign. These patients can be taken for follow up. Women of age >40 years and cyst size of >4 cm are having sanguinous coloured fluid, have increased risk of malignancy. These patients need proper investigation and might need surgical intervention.

KEYWORDS : BREAST CYST, BETA- HCG**INTRODUCTION**

The breast has been a symbol of womanhood and ultimate fertility. Being superficially placed in the body has prompted interest of surgeons since the earliest period in the history of medicine. A few breast diseases occur during reproductive life while some occur during the menopausal period indicating the relation of these diseases to hormonal stimulation as a causative factor.[1] For more than one and a half century the cystic disease of the breast has been recognized as the most frequent female benign breast lesion.[2] Most of the benign epithelial lesions are named by many pathologists with variety of terminologies such as cystic disease, fibrocystic disease, cystic mastitis, cystic mastopathy, epithelial hyperplasia, mammary dysplasia, and benign breast disease.[3] Although some conundrums and controversies exist about the relation between gross cysts and breast cancer, recent evidence suggests that the multidisciplinary study of gross cystic breast disease (GCBD) may be a powerful tool for predicting the natural history of the multifaceted gross cyst pathology. Fibrocystic disease of the breast is thought to result from an inappropriate histologic response to changing hormonal levels. Whether it is indeed a true pathophysiologic disorder is debatable.

Gross breast cysts filled with serous fluid are almost always benign, yet the bearers of such cysts are at four times greater risk of developing a malignancy in the breast. Two forms of benign breast disease have the greatest clinical interest, either for their relationship to neoplasia or for their appearance during particular periods of a woman's maturity. Micronodular fibrocystic disease with ill-defined lumpiness is found with great frequency in young women during pubertal and early reproductive life, whereas gross cysts are most prevalent during the perimenopausal years. The biochemical content of breast cyst fluid (BCF) should reflect the endocrine milieu of the breast. A benign diagnosis allows surgery to be avoided in the majority of cases, while a positive diagnosis of carcinoma allows pre-operative discussion with the patient and proper treatment planning with minimal morbidity.[4]

MATERIALS AND METHODOLOGY

The present prospective analytical study is designed to study the significance of beta-hCG expression in cystic disease of breast. It was conducted at the Department of General Surgery in Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur (CG) from

February 2024 to February 2025. The study population was all females of >18 years age group coming with cystic breast disease at Dr. B.R.A.M. Hospital, Raipur.

Inclusion Criteria

1. Female who gives consent for participating in the study.
2. Patients with no other co morbidities.
3. Patients with cystic lesion of breast.
4. Female patients of > 18yrs age.

Exclusion Criteria

1. Pregnant patients.
2. Patients with ectopic pregnancy, trophoblastic disease, and phantom β -hCG.

The study was approved by the Ethical Committee of the Medical College. Prior to conducting the study. Informed consent was obtained. Material used for the study are Proforma containing patient history, clinical examination, investigations including FNAC Informed consent forms Ultrasonogram and mammogram USG guided aspirate of the breast cyst fluid transferred to a sterile container for transport. This investigation was carried out. Following the acquisition of consent from patients who meet the study's inclusion requirements, clinical evaluations and required investigations are carried out. In order to rule out non-cystic lesions, mastitis, and breast abscess, a clinical breast examination is performed for breast lumps. Mammograms and ultrasounds are performed to detect cystic breast masses. 50 individuals meet the inclusion criteria.

RESULT

Fifty patients who fulfilled the inclusion and exclusion criteria are included into the study during the period of February 2024 to February 2025.

In our study, maximum number of subjects (n=26) was from 31-45 years age group, followed by 18- 30years age group (n=12). We found that mean age group was 40.16 ± 12.45 years. Out of 50 patients, majority of patients (n=33,66%) have chief complain of lump as the primary complain.

In our study, majority of subjects (56%) had right sided breast cyst. Majority of subjects (40%) had cyst in upper outer quadrant of breast followed by upper inner quadrant (28%) of breast.

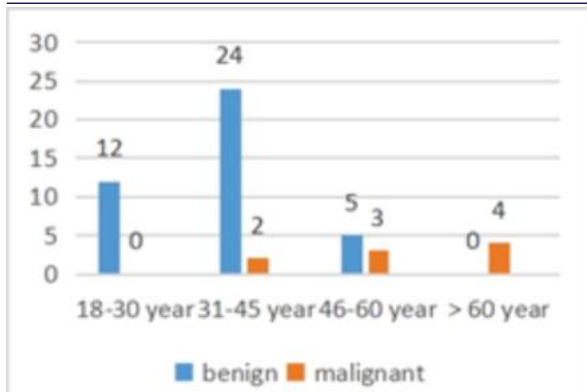


Figure 1: Association Between Age Patient and Histopathology (Benign or Malignant)

Among subjects with 18-30 years (n=12), all subjects had benign cyst. Among patient with 31-45-year age group (26), there were 24 cases (92.3%) were benign, and 2 cases (7.7%) were malignant. Subjects with 46-60-year age group (8) there were 5 cases (62.5%) with benign cyst, and 3 cases (37.5%) with malignant cyst. Among the subjects with age more than 60 years (4) all cases were malignant. The p-value is less than 0.0001 indicates that the size of the cyst was significantly associated with histopathology finding.

Table 1. Showing the Association in Between Breast Cystic Fluid Beta hCG and Histopathology (Benign and Malignant):

Histopathology	BCF BETA HCG		χ^2 (significance)
	less than or equal to 10 mIU/mL	more than 10mIU/mL	
Benign (41)	4 (9.8%)	37 (90.2%)	6.61 (0.01)
Malignant (9)	4 (44.4%)	5 (55.6%)	

The table displays the association of beta hCG levels in breast cystic fluid based on histopathology, distinguishing between benign and malignant cases. Among the benign (41) cases, 37 cases (90.2%) had beta hCG levels greater than 10 mIU/mL, while 4 (9.8%) cases had levels less than or equal to 10 mIU/mL. In malignant cases (9), 4 (44%) had beta hCG levels greater than 10 mIU/mL, while 5 (56%) cases had beta hCG levels less than or equal to 10 mIU/mL. The p-value of 0.01 indicates that benign cysts had a statistically significantly higher level of beta hCG in breast cystic fluid.

Table 2. Association Between Histopathology (Benign and Malignant) and Mean Beta hCG in Breast Cystic Fluid:

HISTOPATHOLOGY	Mean	SD	Unpaired t test (P-value)
BENIGN (41)	33.4	17.3	-0.37 (0.713)
MALIGNANT (9)	36.1	28.1	

The Table shows mean beta hCG level in cystic fluid of benign cysts was 33.4 ± 17.3 mIU/mL and mean beta hCG level in cystic fluid of malignant cysts was 36.1 ± 28.1 mIU/mL. The p-value of 0.713 indicates the level of mean beta hCG in cystic fluid is similar across both benign and malignant breast cyst.

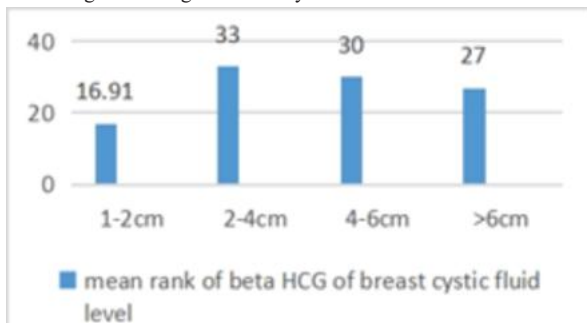


Figure 2: Association Between Mean BCF Beta hCG and Size of Cyst

This table shows the association between the mean of beta hCG level in breast cystic fluid with the size of breast cysts by Kruskal-Wallis's test, and it is lowest in 1-2cm cyst size. Mean of beta hCG level in breast cystic fluid was 16.91, 33.00, 30.00, and 27.00 in 1-2cm, 2-4cm, 4-6cm, and more than 6cm, respectively. The p-value of 0.003 indicates that

the size of the cyst was significantly associated with the level of beta HCG in breast cystic fluid.

The distribution of color of cyst fluid in patients across different histopathology (benign or malignant) was also seen. All patients with clear or straw-colored fluid in cysts were benign and all patients with sanguinous or brownish colored cyst fluid were malignant cysts. The p-value of less than 0.0001 indicates color of cyst fluid was significantly associated with histopathology.

Table 3: Association Between the Size of Cyst and Histopathology (Benign or Malignant):

Size of CYST (n=50)	Histopathology		χ^2 (p-value)
	Benign (41)	Malignant (9)	
1-2 cm (22)	22 (100%)	0	27.61 (<0.001)
2-4 cm (23)	19 (82.6%)	4 (17.4%)	
4-6 cm (3)	0	3 (100%)	
>6 cm (2)	0	2 (100%)	

This table shows the distribution of the size of cysts in patients with benign or malignant breast cyst. All subjects with 1-2cm cyst sizes were benign. Out of 23 subjects, 19 (82.6%) subjects with 2-4 cm of cyst size were benign. All patients with size of 4-6 cm or more than 6 cm cyst were malignant cysts. The p-value of less than 0.0001 indicates size of the cyst was significantly associated with the histopathology of the cyst.

The distribution of the color of breast cyst fluid across different cyst sizes. Among subjects with clear fluid in cyst (n=22), there were 16 cases (72.7%) that had size of 1-2 cm cyst, and 6 cases (27.3%) with size of 2-4cm. Subjects with straw-colored cystic fluid (19), there were 6 cases (31.6%) with size of 1-2 cm, and 13 cases (68.4%) with cyst size of 2-4 cm. Subjects with sanguinous fluid (6) there were 3 case (50%) that had 2-4 cm cyst size, 2 cases (33.3%) and 1 case (16.7%) of cyst size of more than 6cm. The p-value of less than 0.0001 indicates, the size of the cyst was significantly associated with the color of cystic fluid.

DISCUSSION

Various benign diseases affect breast during the reproductive and menopausal phases, often linked to hormonal changes. Cystic disease is the most common benign breast lesion. They are usually benign; their presence increases the risk of developing cancer.

A prospective analytical study was conducted at the Department of General Surgery in Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital from February 2024 to February 2025, Raipur (CG), to analyse the significance of beta-HCG expression in cystic disease of the breast with histopathological findings among females aged more than 18 years coming with cystic breast disease at Dr. B.R.A.M. Hospital, Raipur.

In our study, subjects were from age group from > 18 years. Minimum age of a subject was 21 year and maximum age was 76year. The mean age was 40.16 ± 12.45 years. Maximum patients were from 31-45 years of age group (n=26; 52%). The findings are similar to other studies conducted by Haaggensen et al. [5], Johansson et al. [6], and Hineset al. [7]. But study done by Olarinoye- akorede et al [8] and Venkata Sruthi et al. [9] most common age group was 20-29 years of age. This suggests that Cystic diseases of breast have more prevalence in middle aged women. In our study, most of the patients were from the urban areas (n=50:72%). Most of the patient presented with chief complaint of lump in the breast (n=33; 66%). Pain in breast was chief complaint in 28% (n=14) of patients. The finding was similar to other study done by Kowalski et al. [10], and Kulkarni et al and Olarinoye-akorede et al. [8] This suggests that majority of patients present with palpable mass in breast. In study done by Bhate et al. [11], breast cysts are usually discovered incidentally, with only 20% of cysts being found in women with cyclical mastalgia. In study done by Perry et al. [12], where fibrocystic disease presented with palpable breast lump in 95% of cases.

In our study 74% of the females with breast cyst were multiparous and rest 26% were nulliparous. This finding was inconsistent with previous studies. Studies done by Johansson et al [6] and Kowalski et al. [10] have shown that nulliparity is linked to an increased risk of breast cyst and the risk of breast cysts generally decreases with increasing parity.

In our study most of the patients presented with right sided breast cyst

56% (28/50). Left sided breast cyst was presented by 36% (18/50) and bilateral 8% (4/50). Most of the patient presented with lump in upper and outer quadrant of breast 40% (20/50) and second most common was upper and inner quadrant of the breast 28% (14/50).

In our study, majority of patients had breast cyst of size of 2 – 4 cm (n=23;46%). Only 2 patients had cyst size of more than 6 cm in dimension (4%). Color of cyst fluid was also analyzed and color of cyst fluid were clear fluid (n=22;44%), straw colored (n=19; 38%), brownish (n=3;6%) and sanguinous (n=6; 12%).

In our study, out of 50 cases majority had BIRADS II (n=25; 50%) score in ultrasonography. In studies done by Hines et al. [7] and Sklair-Levy et al. [13] have found that Ultrasound exceeds mammography and clinical palpation in distinguishing the breast cysts.

On histopathological examination via true cyst biopsy malignancy was found in 9 patients (18%) and rest of the breast cyst was found to be benign (n=41; 82%). All the patients with malignant breast cyst had age of more than 40 years. In study done by Venkata Sruthi et al.[9] 43 out of 50 patients with cystic breast lump had benign pathology constituting about 90% of the study population whereas only 7 patients have malignant pathology. This implies most cystic breast diseases are benign.

In this study, distribution of the color of breast cyst fluid across different cyst sizes was done. Among patient with clear fluid in cyst (22), most of the cases (n=16;72.7%) had size of 1-2 cm cyst. 19 patients with straw-colored cystic fluid, out of which 13 cases (68.4%) are having cyst size of 2-4 cm. Among the six patients with sanguinous fluid, there were 3 cases (50%) that had cyst size of 2-4 cm. Patient with brownish fluid (3) there was 1 case (33.3%) that had 2-4cm of cyst size, 1 case (33.3%) that had 4-6 cm of cyst size and 1 case (33.3%) had size of more than 6cm.

In our study, comparison between the size of cyst and histopathology (benign or malignant) was done. All patients with 1-2cm cysts size were benign. Patients with 2-4 cm cyst size 82.6% were benign. All patients with cyst size of 4-6 cm or more than 6 cm cyst were malignant cysts. Therefore, size of the cyst was significantly associated with the histopathology of the cyst. In our study, distribution of colour of cyst fluid in patients across different histopathology (benign or malignant) was observed. It was found that all patients with clear or straw colour fluid in cysts was benign, and all patients with sanguinous or brownish cystic fluid had malignant cysts. Similar finding was found in the studies done by Pokla et al. [14] and Sauter et al. [15]. In study by Lucas et al [16] it was found that if clear fluid is aspirated and the mass resolves, malignancy is unlikely. In this situation, re-evaluation in four to six weeks is appropriate.

In our study we found that beta hCG in breast cyst fluid was increased (>10 mIU/mL) in majority of patients (n = 42; 84%). Only 8 patients had beta HCG in breast cyst fluid less than 10 mIU/mL. Beta hCG was found to be as high as 76.4 mIU/mL and as low as 5.9 mIU/mL. In study by Abney et al. [17] The levels of immunoreactive beta-hCG found in BCF (n = 129) ranged from undetectable levels (<5 mIU/ml) to levels as high as 1432 mIU/ml, with a mean of 58.9 ± 16.8 . In study by Troccoli et al. [18] 66.7% of cases showed high levels of HCG in breast cyst fluid, above normal sera levels. However, vast differences in concentration were found within these high levels. Bradlow et al. [19] have demonstrated high levels of HCG in breast cyst fluids which do not relate to circulating serum levels. The results in patients with multiple cysts showed considerable differences in HCG levels. In our study, Comparison was done between mean BETA -HCG in breast cystic fluid and size of cyst. Mean of beta hCG level in breast cyst fluid was 16.91 mIU/mL, 33.0 mIU/mL, 30.00mIU/mL, and 27.0 mIU/mL in 1-2cm, 2-4cm, 4-6cm, and more than 6cm, respectively. This indicates that the cyst size of 1-2cm had significantly less level of beta HCG in breast cystic fluid.

In our study, comparison was done between breast cystic fluid beta hCG and colour of cyst fluid. 22 cases had clear fluid in breast cyst, out of which 18 cases had beta hCG level greater than 10 mIU/mL. All cases having straw coloured fluid had beta hCG levels greater than 10 mIU/mL. While 2 cases with sanguinous fluid and 2 case with brownish coloured fluid had levels less than or equal to 10 mIU/mL.

In our study, comparison was done between histopathology (benign and malignant) and mean serum beta hCG. Mean serum beta hCG level

in benign cyst was 1.67 ± 1.66 mIU/mL and mean serum beta hCG level in malignant cases was 3.18 ± 3.1 mIU/mL. But all cases had serum beta hCG less than 10 mIU/mL. In study done by Mishra et al. [20], Giorgio Secreto et al. [21] and Mohammed et al. [22] serum beta hcg had no correlation with breast cyst. In study done by Abney et al. [17] All serum beta hCG samples were at the lowest level of detection as compared to beta hCG in breast cyst fluid.

In our study, comparison was done between breast cyst fluid beta hcg, and histopathology (benign and malignant). Among the benign (41) cases, 37 (90.2%) cases had beta hCG levels 57 greater than 10 mIU/mL. In malignant cases (9), 4 (44%) patients had beta hCG levels greater than 10 mIU/mL, while 5 (56%) cases had levels less than or equal to 10 mIU/mL. This indicates that majority of patients with benign breast cyst had beta hcg level higher than 10 mIU/mL. Similar finding was seen in study done by Janssens et al. [23]. In study by Venkata Sruthi et al [9] elevated β -hCG levels were found in approximately 86% of individuals with benign cystic breast disease.

Our study had also compared between mean beta HCG in breast cyst fluid and Histopathology. Mean beta hCG level in cystic fluid of benign cyst was 33.4 ± 17.3 mIU/mL and mean beta hCG level in cystic fluid of malignant cases was 36.1 ± 28.1 mIU/mL. This indicates the level of mean beta HCG in cystic fluid is similar across different types of histopathological characteristic of cyst.

CONCLUSION

Most common chief complaint associated with breast cyst is a lump. Breast cyst of size 1-2cm are majorly having clear fluid are benign and having significantly less value of BCF beta hCG. These patients don't need intervention and can be taken up for follow up with ultrasonography or mammography.

Women of age >40 yrs and cyst size of more than 4 cm are having brownish or sanguinous coloured fluid, have increased risk of malignancy. Although mean beta HCG in cystic fluid is similar across both benign and malignant disease. Serum beta-hCG has no correlation with benign and malignant in cystic diseases of breast.

Unfortunately, in this study the number of patients having malignant breast cyst lesions were very less and time period for follow up is short. In any case, cyst and cancer can coexist. Hence, all gross clinical cysts should be successfully aspirated to demonstrate that they are indeed benign.

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Conflicts of Interest: Nil

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